REMARKS

Claims 397-419 were pending. The Examiner rejected claims 397-419. Applicants have herein cancelled claims 397-412, and 417-419 without prejudice to further prosecution in one or more continuation or divisional applications, amended claims 413 and 416, and added new claims 420-422. The amended and new claims find support in the specification as filed and in priority document U.S. Ser. No. 10/395,001; *see, e.g.*, paragraphs [0010], [0036], and [0038] and the original claims of priority document U.S. Ser. No. 10/395,001. Accordingly, no new matter has been added. After entry of the amendments herein, claims 413-416, 420-422 will be pending.

Applicants thank the Examiner for the acknowledgment that claims 413-415 and partially claim 416 were entitled to claim priority to U.S. Ser. No. 10/395,001.

Information Disclosure Statement

In response to the Examiner's comments on references MU 7900158-OU, MU 7900159-9U, and the reference "Salvador Claro Neto *et al.*," Applicants submit herein abstracts in English and bibliography data corresponding to BR 7900158 and BR 79001159. Applicants also note that the Neto reference English translation had been previously provided in the IDS, but is also included herein for the Examiner's convenience.

Rejections under 35 U.S.C. § 112, 2nd para.

The Examiner rejected claims 397-408 as indefinite. Applicants respectfully disagree, but has cancelled the claims without prejudice in order to further prosecution, thus rendering the rejections moot. Applicant reserves the right to pursue claims to cancelled subject matter in one or more continuation or divisional applications. Withdrawal of the rejections is respectfully requested.

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 413-416 as obvious over Ignacio (Rev. Bras. Ortop., Vol. 32, No. 10 (1997)) ("Ignacio") in view of Arnett (U.S. pat. 6,506,217) ("Arnett"). In particular, the Examiner acknowledged that Ignacio did not teach the step of manipulating a bone scaffold composition *in situ* using external pressure applied to the skin after administration of the composition. The Examiner alleged, however, that Arnett teaches the implantation of a bone filler and bone conforming material wherein after surgery, the surgeon can apply pressure to skin, muscle, or tissue of the patient to contour the bone filler/bone conforming material to mold or shape it, and thus that it would be conventional to apply pressure after implantation to mold or shape an implant.

Applicants respectfully disagree with the rejections as applied to the presently pending claims. Present claim 413, as amended, recites:

> A method, comprising:
>
> administering, through a skin of a patient in need thereof, a partially polymerized, flowable polyurethane bone scaffold composition in or near a bone defect;
>
> manipulating said bone scaffold composition *in situ* using external pressure applied to the skin of the patient; and thereafter,
>
> allowing said bone scaffold composition to become fully cured *in situ*.

Obviousness under § 103 requires consideration of the factors set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), including an analysis of the scope and content of the prior art and the differences between the claimed subject matter and the prior art. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007). Given the differences between the present claims and the cited art, the cited combination of references does not render the present claims obvious, and the Examiner has not met the Office's burden of establishing a *prima facie* case of obviousness.

As acknowledged by the Examiner, Ignacio does not teach or suggest to manipulate a bone scaffold composition *in situ* using external pressure applied to the skin of the patient after administration of the composition. Furthermore, Ignacio does not teach administration of its

compositions *through the skin* of a patient; instead, Ignacio teaches surgical resection of a bone segment of the radii from animals and replacement of the segment with a cylinder made of its compositions. Given that Ignacio implants a "cylinder" of its composition, Ignacio also does not teach administration of a partially polymerized, flowable composition, as presently claimed. At no point does Ignacio teach or suggest that its compositions could be administered through the skin, nor does Ignacio teach or suggest that one having ordinary skill in the art should administer its compositions in partially polymerized, flowable states.

Arnett does not cure the deficiencies of Ignacio. In particular, Arnett discloses that its bone conforming implant compositions are hardened and largely cured *prior to* implantation, such that they are "mineralized solids" after drying and curing, as opposed to the compositions of the present claims, which are implanted when they are partially polymerized and flowable; *see* Arnett, Col. 3, lines 58-67; Col. 4, lines 1-6; and Arnett, Example 2 ("Implanting the Hardened Implant"). Arnett states, in fact, that in attempts to eliminate the first step of hardening the compositions, the results were not optimal because the unhardened composition would become "very soggy" and "would not hold a desired shape." Indeed, such unhardened implants of Arnett, after implantation, tended to be flattened out by the pressure of the surgical site tissue once the surgical site was closed. Only *after* hardening its compositions to such a "mineralized solid" state and implanting them, would Arnett then apply pressure to further mold the implant. *See* Arnett, Col. 4, lines 1-48 and Example 3. Accordingly, Applicants respectfully assert that Arnett in fact teaches away from the presently claimed methods, as the reference clearly directs the skilled artisan away from the use of a flowable or unhardened implant.

Furthermore, Arnett also only teaches surgical implantation of its hardened compositions *in situ*, *i.e.*, on exposed bone after removal of overlying tissue, rather than administration through the skin of a patient, as required by the present claims. *See* Arnett, Col. 4, lines 5-27 and Example 2. As one having ordinary skill in the art would recognize, implantation of a hardened composition (*e.g.*, either the Ignacio or Arnett compositions) through the skin of a patient might be technically difficult to achieve and might result in significant patient pain.

Given the teachings of Ignacio and Arnett, one having ordinary skill in the art would not have been prompted to modify the methods of Ignacio with Arnett to result in the presently claimed methods. Neither reference teaches or suggests administration of a partially polymerized, flowable composition through the skin of a patient, either alone or in combination. Indeed, Arnett discloses that implantation of a bone conforming material that was not hardened and cured to a mineralized solid state was not optimal and yielded an implant that would not hold a desired shape. A person having ordinary skill in the art would thus not have a reasonable expectation of success that modification of the Ignacio methods with those of Arnett would result in a useful method of bone repair.

Applicants note that the cancellation, without prejudice, of claims 397-412 and 417-419 renders the additional rejections under 35 U.S.C. § 103 moot. Applicants reserve the right to pursue the cancelled subject matter in one or more continuation or divisional applications.

Given all of the above, Applicants respectfully assert that the pending claims are not obvious and request withdrawal of the rejections.

CONCLUSION

Applicants respectfully assert that the pending claims are in condition for allowance, which action is hereby requested. The Examiner is invited to telephone the undersigned if such would expedite prosecution.

Enclosed is a Petition for Extension of Time fee (3 months). Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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